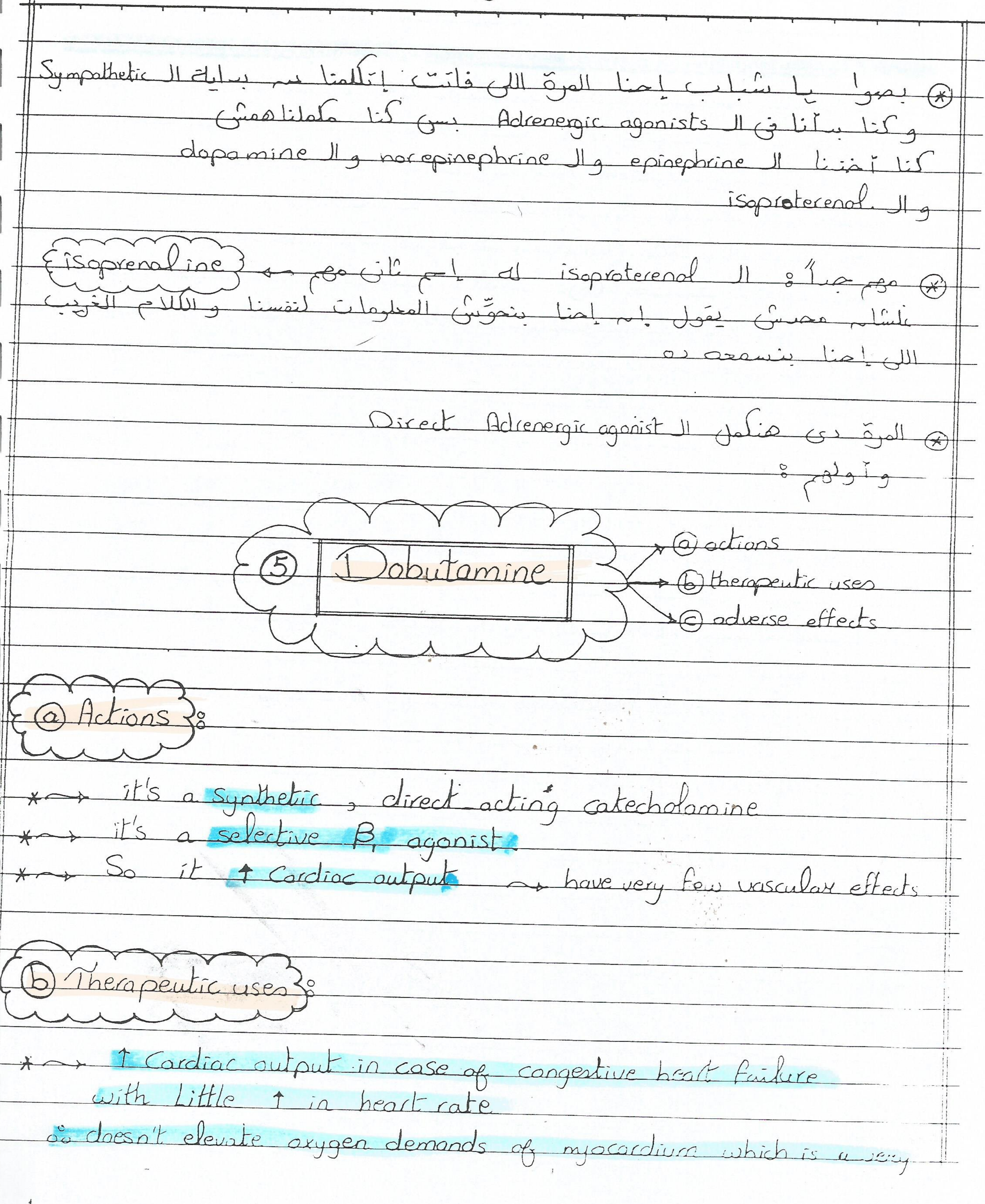
د/ أنس h.(7) والاخيرة





* بصوا يا شباب إحنا المرة اللي فاتت إتكلمنا عن بداية الـ Sympathetic وكنا بدأنا في الـ Adrenergic agonists بس كنا مكملناهمش كنا أخدنا الـ epinephrine والـ norepinephrine والـ dopamine والـ isoproterenol.

* مهم جداً: الـ isoproterenol له إسم تاني مهم ← {isoprenaline} علشان محدش يقول إسم إحنا بنحوّش المعلومات لنفسنا والكلام الغريب اللي إحنا بنسمعه ده

* المرة دي هنكمل الـ Direct Adrenergic agonist وأولهم:

## ⑤ 1 Dobutamine

→ ⓐ actions
→ ⓑ therapeutic uses
→ ⓒ adverse effects

### ⓐ Actions:

* → it's a synthetic, direct acting catecholamine
* → it's a selective $B_1$ agonist.
* → So it ↑ Cardiac output → have very few vascular effects

### ⓑ Therapeutic uses:

* → ↑ Cardiac output in case of congestive heart failure with Little ↑ in heart rate.

∴ doesn't elevate oxygen demands of myocardium which is a very

important advantage over other sympathomimetic drugs.

← بص يا حبيبي ← دلوقتي أنا زودت الـ COP ← مع إني ما زودتش الـ HR أوي

← يبقى أكيد أنا زودت الـ stroke volume

$$COP = \text{Strock vol} \times HR$$

لأن الـ HR زادت بنسبة قليلة ← لذلك مجهود عضلة القلب لم يزد أوي وهو ده اللي أنا عايزه علشان الـ oxygen demand لعضلة القلب نفسها مايزيدش ← وده طبعاً في حالة إن أنا يكون عندي مشكلة في الـ coronary arteries اللي بتجيب الدم والـ oxygen لعضلة القلب نفسها علشان تتغذى وتشتغل

Ⓒ Adverse effects :

① should be used with caution in case of atrial fibrillation, as it ↑ the A.V. Conduction

يعني علشان الـ fibrillation اللي في الـ Atria ماتوصلش الـ ventricles تبقى مصيبة

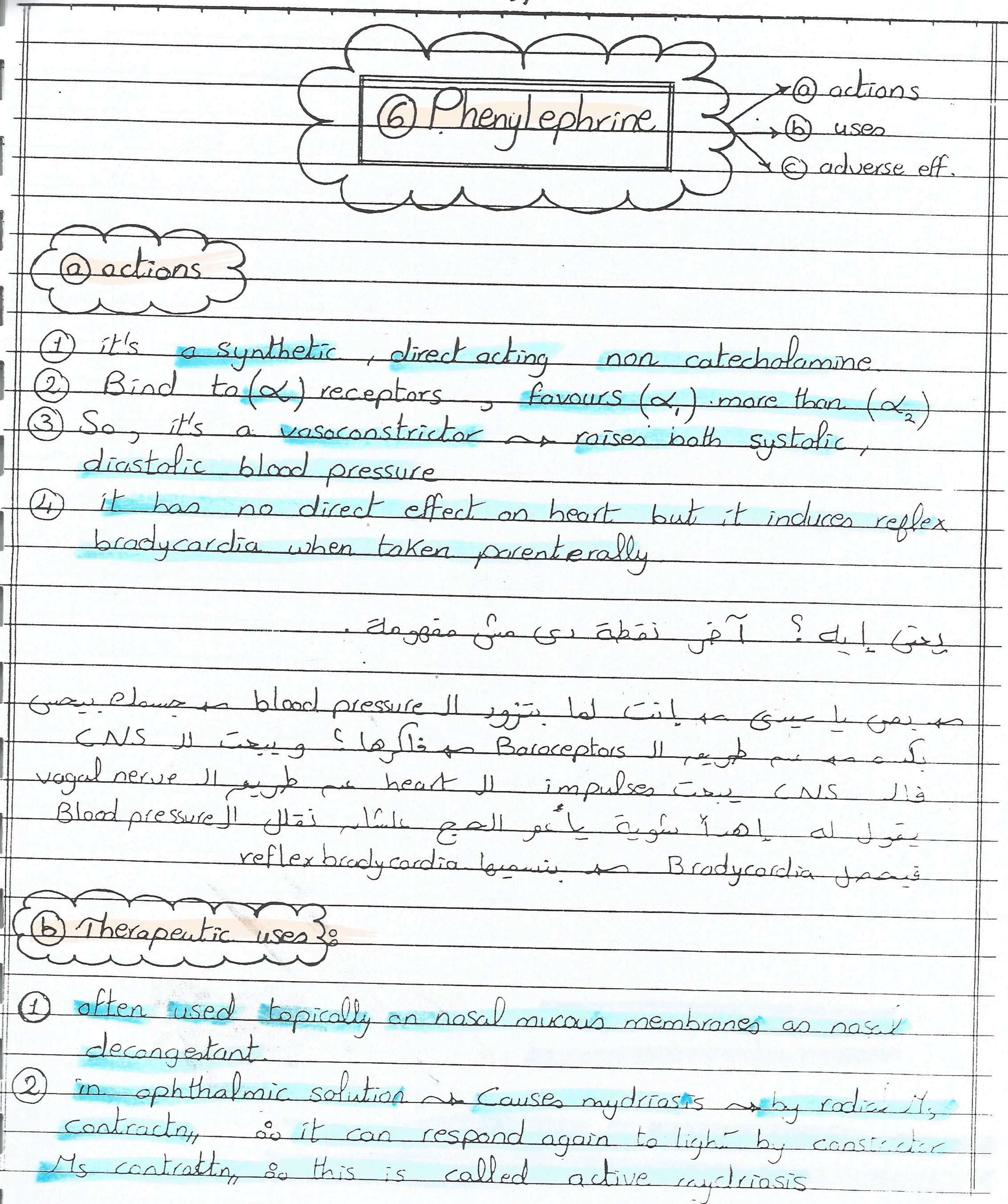
② Tolerance may develop on prolonged use

③ other adverse effects like those of epinephrine may develop

Pray alot for US

PLZZZZZZ ...

2B1



# ⑥ Phenylephrine

→ ⓐ actions
→ ⓑ uses
→ ⓒ adverse eff.

## ⓐ actions

1. it's a synthetic, direct acting non catecholamine.
2. Bind to ($\alpha$) receptors, favours ($\alpha_1$) more than ($\alpha_2$)
3. So, it's a vasoconstrictor → raises both systolic, diastolic blood pressure
4. it has no direct effect on heart but it induces reflex bradycardia when taken parenterally

يعني إيه؟ آخر نقطة دي مش مفهومة.

بص يا سيدي ← إنت لما بتزود الـ blood pressure ← جسمك بيحس
بكده عن طريق الـ Baroceptors ← فاكرها؟ وبيبعت للـ CNS
فالـ CNS بيبعت impulses للـ heart عن طريق الـ vagal nerve
يقول له اهدا شوية يا عم الحج علشان نقلل الـ Blood pressure
فيحصل Bradycardia ← بنسميها reflex bradycardia

## ⓑ Therapeutic uses:

1. often used topically on nasal mucous membranes as nasal decongestant.
2. in ophthalmic solution → Causes mydriasis → by radial Ms contraction, ∴ it can respond again to light by constrictor Ms contraction, ∴ this is called active mydriasis

# II non Catechdamine

① phenyl ephrine

② methoxamine

③ clonidine

④ metaproterend

## I phenyl Ephrine (synthetic)

### A Actn

- more potent $\alpha_1 > \alpha_2$
- vaso constrictn
- ↑ SBP ↑ DBP

N.B has no Direct effect on heart but ↑ reflex brady Cardia when Taken Parenterally → ??? why

### B Therapeutical use

① Topically → nasal Congestant
→ opthalmic prep.

To make Active mydriasis

???

responsive To light

i.e not block for Constrictor Muscule

### C Adverse effect

① hyperTension

② Head ache

③ Cardiac irrigularities

N.B phenyl ephrine is non Catechdamine so resiste COMT.

إيه القرف ده يا عم إنت ما تتكلم عربي وتفهمنا

بص يا سيدي حضرتك عندك نوعين من الـ Muscles في الـ eye

① radial Ms ← لو حصلها contraction بالـ (α) ← يحصل Mydriasis

② constrictor Ms ← كنا اتفقنا في الـ Parasymp. Syst لما بتعرض العين لضوء قوي ← الـ constr. Ms بيحصلها contraction فيحصل Meiosis.

كده الـ Mydriasis اللي بيحصل للـ eye في الأول بتسميه active بالشكل لما بتعرضه للضوء بي respond.

← لكن أنا لو عامل Mydriasis عن طريق إني أنا أعمل Blocking للـ receptor بتاع الـ constrict Ms ← فيحصلها relaxation ← ويبعد كده جيت عرضت الـ eye للضوء ← الـ constr. Ms طالما ← فالضوء مش هيأثر عليها ← فهتفضل متعملة Blocking للضوء ← كده بنسمي الـ Mydriasis ده passive Mydriasis

← يا رب تكونوا وصلت ← لو مش فاهم تعالى لنا واحنا نظبطك.

③ This drug is used to raise blood pressure in case of hypotension, to terminate episodes of supraventricular tachycardia (rapid heart arising from A.V. Junction, atria)

## © Adverse effects :

① large doses can cause :
* hypertensive headache.
* Cardiac irregularities.

V.I. N.B. → Phenylephrine isn't a catecholamine derivative ∴ It's not a substrate for catechol-O-Methyl trasferase (COMT)

PhenyL Ephrine →, Cs; [2] methoxamine

• Synthetic

A Actn

• $\alpha_1 > \alpha_2$

• have no Direct effect on heart but ↑ reflex brady cardia

B Therapeutical uses

① Ⅲ of hypotension during surgery ē halothane anesthetics

② relieve attacks of Paroxysmal supra ventricular Tachy cardia

• Terminate episodes of supraventricular Tachycardia

C Adverse effect

- hypertension
- Headach
- Cardiac irrigularities

1) Direct

N.B Selective $\alpha_1$ Agonist

[1] PhenyL Epherine

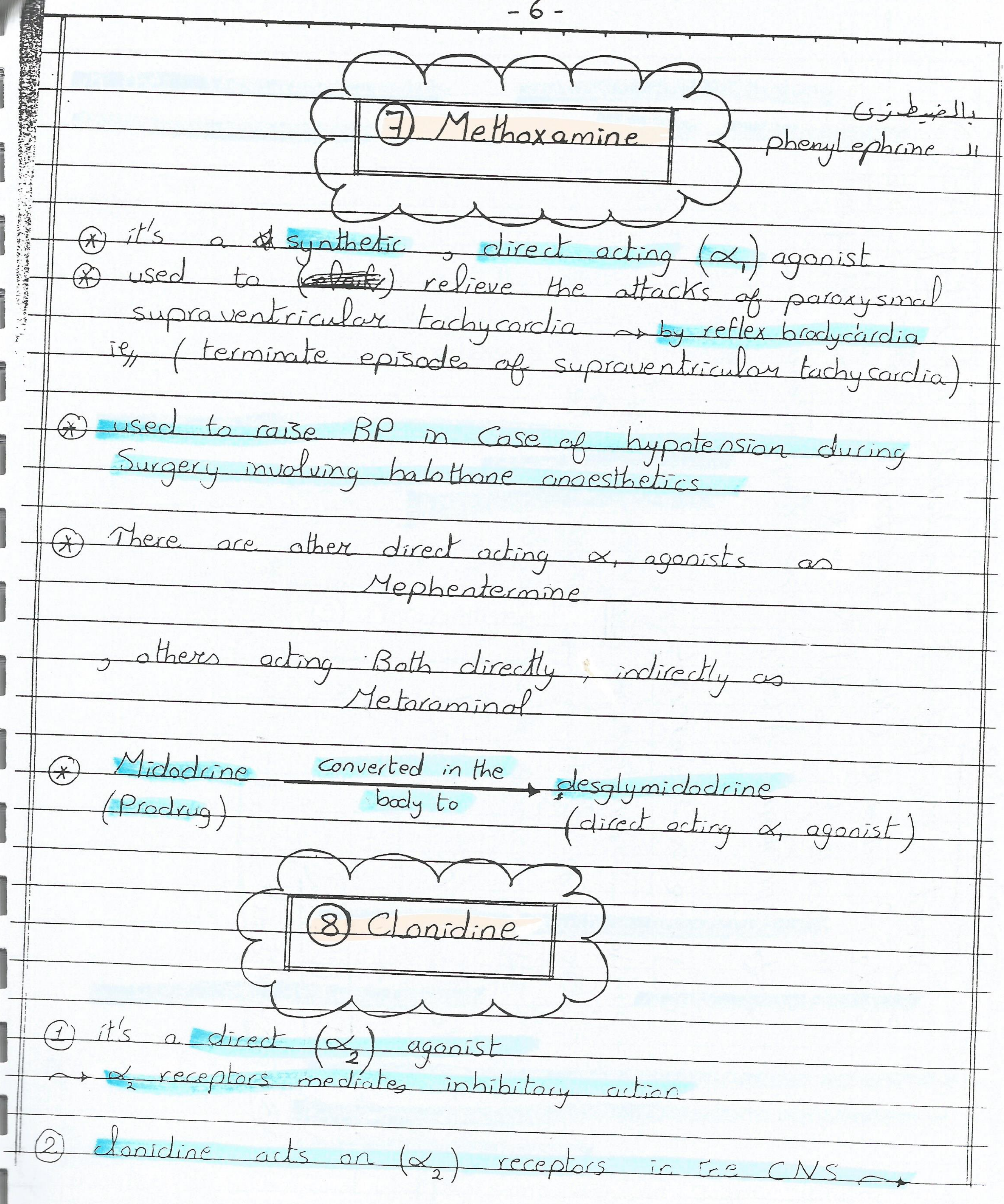
[2] Methoxamine

[3] Mephentermine

[4] Midodrine (prodrug) ↓ desglymidodrine

N.B direct and indirect $\alpha_1$ selective Agonist

Metaraminol



## ⑦ Methoxamine

بالضبط زي phenylephrine ..

- ⊛ it's a synthetic, direct acting ($\alpha_1$) agonist.
- ⊛ used to relieve the attacks of paroxysmal supraventricular tachycardia → by reflex bradycardia
  ie, (terminate episodes of supraventricular tachycardia).
- ⊛ used to raise BP in case of hypotension during surgery involving halothane anaesthetics.
- ⊛ There are other direct acting $\alpha_1$ agonists as
  Mephentermine
  , others acting both directly, indirectly as
  Metaraminol
- ⊛ Midodrine (Prodrug) —converted in the body to→ desglymidodrine (direct acting $\alpha_1$ agonist)

## ⑧ Clonidine

① it's a direct ($\alpha_2$) agonist
→ $\alpha_2$ receptors mediates inhibitory action.

② clonidine acts on ($\alpha_2$) receptors in the CNS →

3 Clonidine

• 1) Direct $\alpha_2$ Agonist (mediated inhibitory Actn)
• $\alpha_2$ R found in CNS in vasometer Center → inhibatn → vasoditatatn → ↓ PR → ↓ BP → Ttt of hypertension
• ↓ symptoms of Diazepines (hypertension)

4 metaproterenol

- Similar Isoproterenol But resist COMT
- Act on $\beta_2$ R → Bronchodilatn
So Ttt of asthma + bronchospasm.

N.B Selective $\beta_2$ Agonist

1- terbutaline
2- Albuterol
3- Salbutamol

in the Vasomotor centre causing its inhibition resulting in vasodilatation → ↓ PR → hypotension

هي حتة عربي هي بتاعت شايك في الـ CNS منطقة اسمها الـ Vasomotor centre
هي دي هي اسمها كده هي مسؤولة عن الـ contraction of B.V.
هي لذلك أنا لو عملت inhibition للـ Vasomotor centre عن طريق الـ $\alpha_2$
هيحصل Vasodilatation هي لذلك هيقل الـ PR وهيحصل hypotension
أو بمعنى أصح هعالج الـ hypertension.

③ it can minimize the symptoms that accompany the withdrawal of opiates or Benzodiazepines
those symptoms are hypertension mainly

## ⑨ Metaproterenol

(*) although it resembles isoproterenol → {But} it's not a catecholamine
∴ it's resistant to COMT

(*) it acts on $B_2$ receptors causing Bronchodilation, improvement of airway function
∴ used in asthma treatment → & reverse bronchospasm.

(*) {Terbutaline} → $B_2$ more selective agonist with longer duration of action → Bronchodilator, reduce uterine contraction in Premature labour

(*) {Albuterol} [Salbutamol] → the same as Terbutaline used as inhalant to relieve bronchospasm.

# B indirect Acting Agonist (indirect sympathomimetics)

→ ↑release of Neurotransmitter from vesicles → effect
↑release of NE from presynaptic Terminals (endogenous NE)

→ Don't Act directly on Post synaptic

ex

## ① Amphetamine

- ↑NE
- Act α → ↑BP
- Act β → ↑CoP

- Abuse

- uses

① Tt of Depression
② " " Narcolepsy
③ Apetite Control

- C-I

in pregnancy
Teratogenic

## ② Tyramine

→ not used clinically
→ found in fermented food
mainly oxidised by monoamine MAO

If Patient ← MAO inhibitor →
↑hypertension → Arrythema.

كده يا شباب حمه إحنا خلصنا كل الـ direct acting adrenergic agonists
يعني كل الحاجات اللي بتدخل حمه تمسك على الـ receptors على طول وتعمل
الـ effect زي الـ Natural Neurotransmitters

ودلوقتي هنبدأ في الـ indirect adrenergic agonists اللي بتيجي على الـ vesicles
وتزود الـ release بتاع الـ Natural neurotransmitters فتزيد الـ effect.

# Indirect - Acting Adrenergic Agonists

(*) They Cause ↑ of norepinephrine released from presynaptic terminals ie,, endogenous NE

(But) → they don't act directly on postsynaptic receptors.

They include :

- Amphetamine
- Tyramine.

## (1) Amphetamine

(*) it acts by ↑ release of catecholamines
∴ ↑ BP by acting on α receptors
, ↑ BP by ↑ heart activity by acting on β receptors

(*) it has CNS stimulatory effect → is often mistaken by drug abusers
يعني بيعمل دماغ عالية

(*) it can be used in treatment of :
(1) depression (2) narcolepsy إحساس دائم بالنعاس
(3) apetite control (4) children hyperactivity مش عارفة بصراحة إزاي

(*) should be avoided during pregnancy due to its effects on fetus development i.e., teratogenic يعمل تشوهات في الجنين

## (2) Tyramine

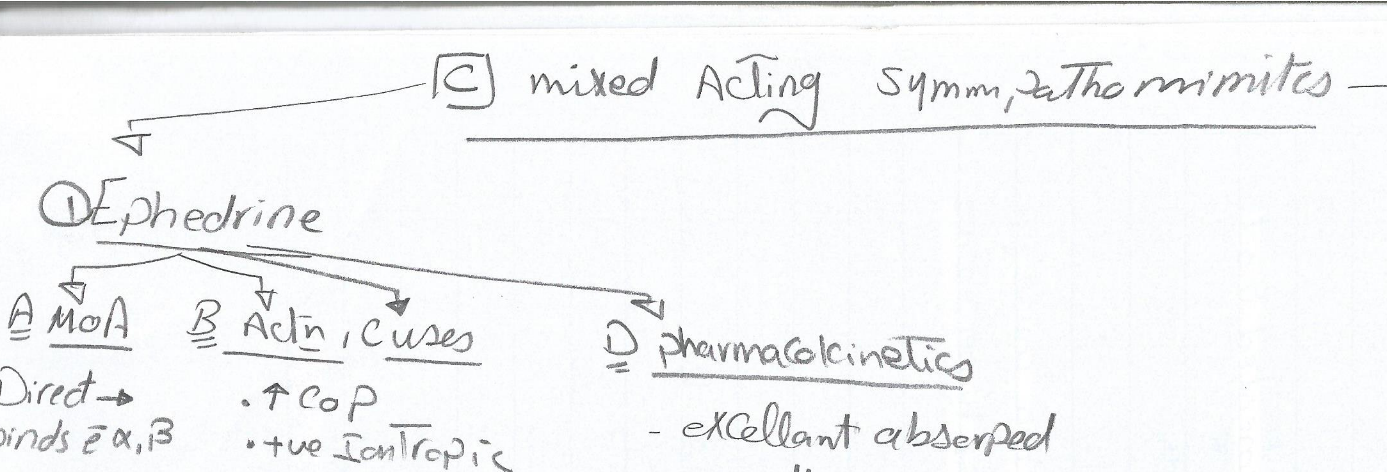
(*) it's not clinically used but found in fermented food as ripe cheese, wine

(*) Normally, it's oxidized by MAO
→ if patient is taking MAO inhibitors → it can cause serious vasopressor episodes (vasoconstrictn → hypertensive crisis)
أزمة
أو مشكلة.
أو مصيبة.

كده إحنا خلصنا ال Indirect adrenergic agonists
هـ تعالوا نشوف آخر نوع من ال agonists وهو ال Mixed adrenergic agonists
يعني ممكن يشتغلوا direct وممكن يشتغلوا indirect

## Mixed acting Adrenergic Agonists

- Ephedrine
- Metaraminol



# C mixed Acting sympathomimetics

## ① Ephedrine

**A MoA**

- Direct → binds ē α, β
- inDirect → ↑ NE release

**B Actn, C uses**

- ↑ COP
- +ve Iontropic
- +ve chronotropic
- ↑ SBP. ↑ DBP
- ① CNS Stimulant (↓ fatigue - sleep)
- ② ↑ Contractn of skeletal muscule + antichdinesterase in myasthenia gravis ???
- ③ Bronchodilator → chronic asma only why??? as prophylactic
- ④ Improves athlete Performance
- ⑤ nasl congestant

**D pharmacokinetics**

- excellant absorped orally
- Penetrate BBB
- resist MAO - COMT as They are Noncatechol amine
- eliminated unchanged in urine.

## ② Metaraminol

④,

- like norepinephrine in Actn
- Ⅲ of shock
- Ⅲ of hypoTension

when NE, Dopamine I-V infus is impossible?

→ I-V as single dose
→ mild vasoconstrictn
→ ↑ COP - ↑ Activity of heart

فاكرينه ص أختناقى
ال phyto صيقى
Plant Alkaloid
تعالوا نشوفه فى الـPharma
هنتكلم عنه إزاى

# (1) Ephedrine

- (a) mechanism of actn.
- (b) PharmacoKinetics.
- (c) actions.
- (d) uses.

## (a) mechanism of actn. :

(*) it can ↑ the release of catecholamines (NE) from presynaptic neurons

(*) also it can Bind directly to α, B receptors
that's why we call it Mixed acting adrenergic agonist

## (b) PharmacoKinetics :

(*) has excellent absorptn. orally

(*) Penetrates BBB → reaches CNS

(*) it's not a catechol ∴ not affected by COMT , MAO
∴ has Longer duratn. of actn. than (NE)

(*) Eliminated unchanged in urine as its not affected by COMT , MAO.

## (c) Actions :

(1) it ↑ both systolic , diastolic BP by ↑ vasoconstrictn. ($\alpha_1$) , ↑ cardiac stimulatn. ($B_1$)

(2) Mild CNS stimulatn. → ↑ alertness , ↓ fatigue , prevent sleep

③ Enhances contractility, improves motor functn in Myasthenia gravis → especially if used with anticholinesterases

فاكر ال myasthenia gravis دي كانت إيه ؟

← أكيد لا

← افتكر ← دي كانت حالة تشبه في ال skeletal Ms relaxatn

كنت بعالجها بإني أدي anticholinesterases علشان أزود ال Ach

على ال Neuromuscular Junctn فأزود ال contractility وأنشط العضلات

قوية

④ it produces Bronchodilatn → (But) → it's less potent than epinephrine, isoproterenol in this effect, slower.

∴ it's Just used prophylactically (للوقاية) in case of chronic asthma → to prevent attacks

∴ it's not used in acute asthma → only chronic

⑤ it improves athlete performance

∴ Banned in (olympic games) علشان كده بيتمنع في الأولمبيات

## ⓓ Uses :

ممكن تستنتجهم من ال actn لو إنت ذكي (حلو)

① to used prophylactically in chronic asthma treatment.
② to raise blood pressure in Cases of hypotension.
③ nasal decongestant → due to its local vasoconstrictor actn

(But) → the clinical use of ephedrine is ↓ due to presence of more potent drugs with fewer adverse effects.

*locally symmpathomimitics

For nasal mucosal membrane, eye

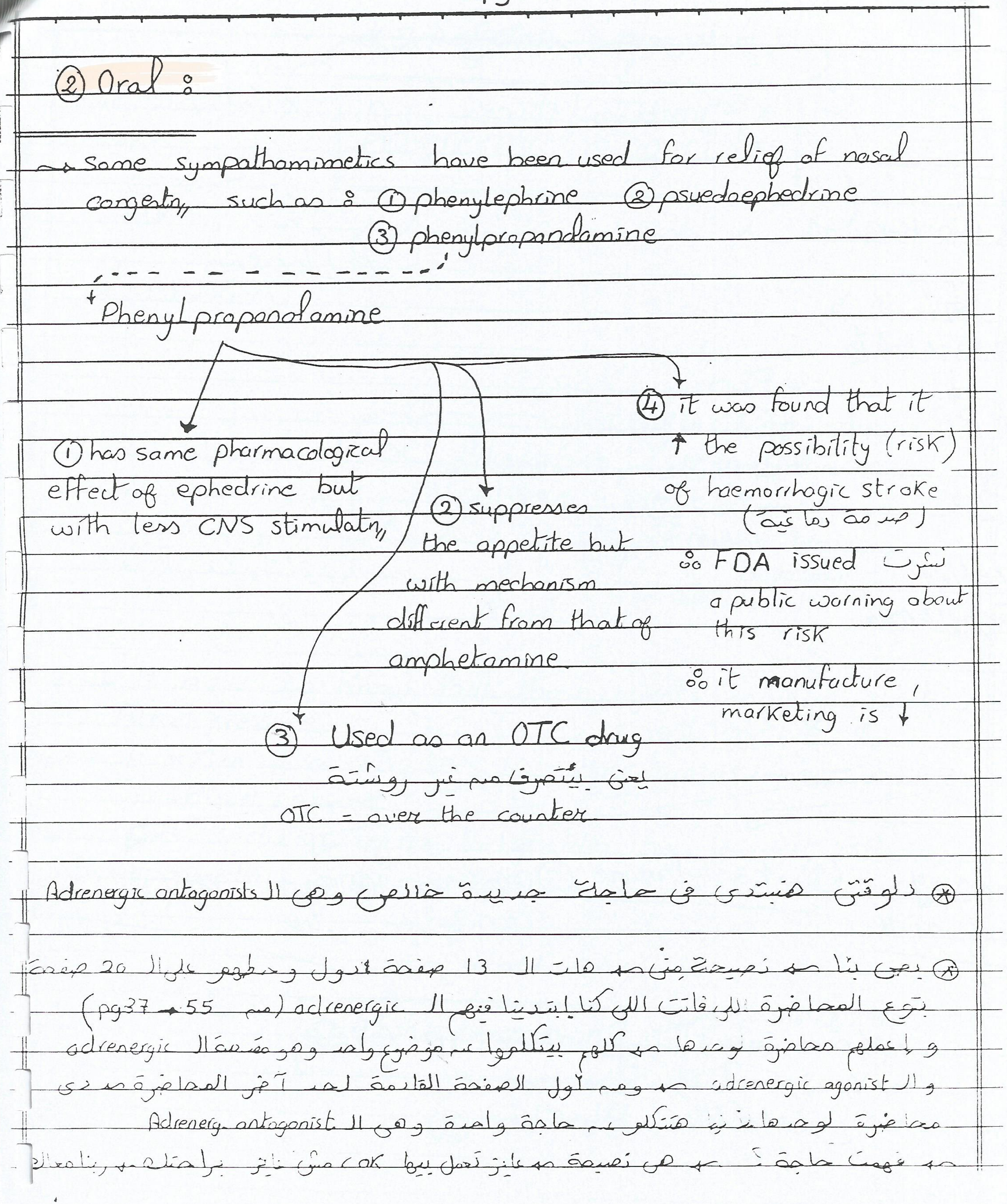
ex 1. oxymetazoline
2- xylometazoline
3- propyl hexedrine

* orally symmpathomimitics

For relief of nasal congestion

ex
1. phenyl Ephrine
2. pseud Ephedrine
3. phenyl propanolamine

- have the same pharmacological effect of Ephedrine but ↓CNS stimulation
- supress the appetite ē mechanism diff from amphetamine
- used as OTC
- risk of haemorrhagic stock هيموراجيك



## ② Oral :

→ some sympathomimetics have been used for relief of nasal congestion, such as : ① phenylephrine ② psuedoephedrine ③ phenylpropanolamine

---

† Phenylpropanolamine

① has same pharmacological effect of ephedrine but with less CNS stimulation

② suppresses the appetite but with mechanism different from that of amphetamine

③ Used as an OTC drug
يعني بيتصرف من غير روشتة
OTC = over the counter

④ it was found that it ↑ the possibility (risk) of haemorrhagic stroke (صدمة دماغية)
∴ FDA issued نشرت a public warning about this risk
∴ it manufacture, marketing is ↓

⊛ دلوقتي هنبتدي في حاجة جديدة خالص وهي الـ Adrenergic antagonists

⊛ يعني بنا ـه نصيحة مني ـه هات الـ 13 صفحة الأول وحطهم على الـ 20 صفحة
بتوع المحاضرة اللي فاتت اللي كنا ابتدينا فيهم الـ adrenergic (من 55 ← pg37)
و اعملهم محاضرة لوحدها ـه كلهم بيتكلموا عن موضوع واحد وهو مقدمة الـ adrenergic
والـ adrenergic agonist ـه ومن أول الصفحة القادمة لحد آخر المحاضرة ـه دي
محاضرة لوحدها ـه هتتكلم عن حاجة واحدة وهي الـ Adrenerg. antagonist
ـه فهمت حاجة ؟ ـه هي نصيحة ـه عايز تعمل بيها OK، مش عايز براحتك يا صاحبي